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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/737,328	12/16/2003	Satoru Kuhara	JG-YY-4946D-C/500569.	6127

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/737,328	KUHARA ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-18 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/499,717.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE filed on November 3, 2005 and the amendment filed on September 19, 2005 have been entered. The claims pending in this application are claims 14-18 and 22-25. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on September 19, 2005.

Claim Objections

2. Claim 14 is objected to because of the following informalities: (1) "heating or exposing the carrier to radiation" in lines 8 and 9 should be "heating the carrier or exposing the carrier to radiation"; (2) "said oligonucleotide and polynucleotide" in lines 6 and 7 should be "said oligonucleotide or polynucleotide".

3. Claim 16 is objected to because of the following informality: "heating or exposing the carrier to radiation" in last line should be "heating the carrier or exposing the carrier to radiation".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Enablement

Claims 14-18 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods recited in claims 14-18 and 22-25 can be performed using a carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability how the method recited in claims

14-18 and 22-25 can be performed using a carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine.

Claim 14 is directed to a method of fixed an oligonucleotide or a polynucleotide to a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine and can be read as a method of fixed an oligonucleotide or a polynucleotide having an amino group to a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier. Claim 15 further limits claim 14 and requires that the oligonucleotide or the polynucleotide is fixed to the solid carrier at its one end portion. The specification does not provide a guidance to show that an oligonucleotide or a polynucleotide having an amino group can be fixed to a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier. Since it is known in the art that polylysine, polyethylene imine and polyalkylamine carries multiple amino groups (NH_2) (see Figure 1 in Running *et al.,* BioTechniques, 8, 276 and 279, 1990; Figure 1 in Bastardo *et al.,* J. Phys. Chem. B, 109, 167 -174, 2005; column 5, lines 51-67 and column 6, lines 1-8 in US Patent No. 4,775,619), a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine must carry multiple positive charges. Therefore, it is unclear how an oligonucleotide or a polynucleotide having an amino group is fixed to a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier as recited in claims 14 and 15.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether an oligonucleotide or a polynucleotide having an amino group can be fixed to a solid carrier coated with poly-l-lysine, polyethylene imine or polyalkylamine by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown *et al.,* (US Patent No. 5,807,522, filed on June 7, 1995) in view of Cook (US Patent No. 6,017,895, filed on February 10, 1992).

Note that this rejection is based on that one of lambda clone PCR products is considered as a hydrophilic polymer since lambda clone products are water-soluble and that an oligonucleotide or a polynucleotide having an amino group is not fixed to the solid carrier by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier.

Regarding claims 14 and 16-18, since Brown *et al.,* teach to load 1 μl of the concentrated lambda clone PCR product in 3 ×SSC directly from 96 well storage plates into the open capillary printing element and deposit about ~5 nl of sample per glass slide at 380 micron spacing between spots, on each of 40 slides wherein the slides are coated with a layer of poly-l-lysine (see column 16) and claim 14 does not require that a hydrophilic polymer and a compound must be different, Brown *et al.,* disclose pretreating the carrier with poly-l-lysine, spotting an aqueous solution containing a hydrophilic polymer (ie., the concentrated lambda clone PCR product) and a compound selected from the group consisting of the oligonucleotide and polynucleotide (ie., the concentrated lambda clone PCR product) onto the pretreated solid carrier (ie., the glass slide coated with poly-l-lysine), said oligonucleotide or polynucleotide thereby fixing the compound to the solid carrier by electrostatic bonding (ie., by the interaction between the concentrated lambda clone PCR product with negative charges and poly-l-lysine with positive charges) wherein the solid carrier is a glass sheet as recited in claims 14, 17, and 18. Since Brown *et al.,* teach that, after the spotting operation is complete, the slides are rehydrated in a humid chamber for 2 hours, baked in a dry 80° C vacuum oven for 2 hours, rinsed to remove unabsorbed DNA, and then treated with succinic anhydride to reduce non-specific adsorption of the labeled hybridization probe to the poly-l-lysine coated glass surface and immediately prior to use, the

immobilized DNA on the array is denatured in distilled water at 90°C for 2 minutes (see column 16), Brown *et al.,* disclose washing the carrier (ie., rinsing to remove unabsorbed DNA), drying the carrier (ie., baking in a dry 80°C vacuum oven), and heating the carrier as recited in claim 14 wherein washing the carrier resulting from the spotting step and drying the carrier resulting from the washing step prior to heating the carrier (ie., incubating the array at 90°C for 2 minutes) as recited in claim 16.

Brown *et al.,* do not disclose that said oligonucleotide or polynucleotide has an amino group as recited in claim 14.

Cook teaches that oligonucleotides have certain modifications to the 3' or 5' terminus to improve the pharmacological properties of the oligonucleotides wherein the modifications include amino groups, polyethylene glycol, polylysine, acridine, dodecanol, long chain aliphatic groups and cholesterol (see column 3, lines 31-35).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claim 14 wherein said oligonucleotide or polynucleotide has an amino group in view of the prior art of Brown *et al.,* and Cook. One having ordinary skill in the art would have been motivated to do so because Cook suggests that certain modifications (ie., adding an amino group) to the 3' or 5' terminus of oligonucleotides would improve the pharmacological properties of the oligonucleotides (see column 3, lines 31-35) and the simple replacement of one kind of oligonucleotide (i.e., the PCR product taught by Brown *et al.,*) from another kind of oligonucleotide (i.e., the oligonucleotide having an amino group on its 3' or 5' taught by Cook) during the process for performing the method recited in claim 14 would have been, in the absence of convincing evidence to the

contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the PCR product taught by Brown *et al.*, and the oligonucleotide taught by Cook have the same intended use (ie., loaded onto a solid support).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07, and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

8. Claims 14, 16-18, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown *et al.*, in view of Cook and Rudolph (EP 320842 A2, published on December 12, 1988).

Note that this rejection is based on that a hydrophilic polymer is different from one of lambda clone PCR products and that an oligonucleotide or a polynucleotide having an amino group is not fixed to the solid carrier by electrostatic bonding between the amino group and poly-l-lysine, polyethylene imine or polyalkylamine on the carrier.

Regarding claims 14 and 16-18, since Brown *et al.*, teach to load 1 μl of the concentrated lambda clone PCR product in 3 ×SSC directly from 96 well storage plates into the open capillary printing element and deposit about ~5 nl of sample per glass slide at 380 micron spacing between spots, on each of 40 slides wherein the slides are coated with a layer of poly-l-lysine (see column

16), Brown *et al.*, disclose pretreating the carrier with poly-l-lysine, spotting an aqueous solution containing a compound selected from the group consisting of the oligonucleotide and polynucleotide (ie., the concentrated lambda clone PCR product) onto the pretreated solid carrier (ie., the glass slide coated with poly-l-lysine), said oligonucleotide or polynucleotide thereby fixing the compound to the solid carrier by electrostatic bonding (ie., by the interaction between the concentrated lambda clone PCR product with negative charges and poly-l-lysine with positive charges) wherein the solid carrier is a glass sheet as recited in claims 14, 17, and 18. Since Brown *et al.*, teach that, after the spotting operation is complete, the slides are rehydrated in a humid chamber for 2 hours, baked in a dry 80° C vacuum oven for 2 hours, rinsed to remove unabsorbed DNA, and then treated with succinic anhydride to reduce non-specific adsorption of the labeled hybridization probe to the poly-l-lysine coated glass surface and immediately prior to use, the immobilized DNA on the array is denatured in distilled water at 90°C for 2 minutes (see column 16), Brown *et al.*, disclose washing the carrier (ie., rinsing to remove unabsorbed DNA), drying the carrier (ie., baking in a dry 80°C vacuum oven), and heating the carrier as recited in claim 14 wherein washing the carrier resulting from the spotting step and drying the carrier resulting from the washing step prior to heating the carrier (ie., incubating the array at 90°C for 2 minutes) as recited in claim 16.

Brown *et al.*, do not disclose an aqueous solution containing a hydrophilic polymer and a compound selected from the group consisting of the oligonucleotide and polynucleotide wherein said oligonucleotide or polynucleotide has an amino group as recited in claim 14 and wherein the hydrophilic polymer is a nonionic polymer or a cationic polymer as recited in claim 22 and hydrophilic polymer is a cellulose derivative as recited in claim 23, wherein the hydrophilic

polymer is selected from the group consisting of polyacrylamide, polyethylene glycol, polyvinyl alcohol and saccharide as recited in claim 24, and wherein the aqueous solution contains the hydrophilic polymer in an amount of 0.1 to 2.0 vol. % as recited in claim 25.

Regarding claim 14, Cook teaches that oligonucleotides have certain modifications to the 3' or 5' terminus to improve the pharmacological properties of the oligonucleotides wherein the modifications include amino groups, polyethylene glycol, polylysine, acridine, dodecanol, long chain aliphatic groups and cholesterol (see column 3, lines 31-35).

Regarding claims 14 and 22-25, since Rudolph teaches to load RNA or DNA probes with a binding aid onto a solid support and teaches that useful binding aids includes cellulose derivatives, starch, and polysaccharides and 1% binding aid solution is suitable (see columns 2-4), Rudolph disclose an aqueous solution containing a hydrophilic polymer and a compound selected from the group consisting of the oligonucleotide and polynucleotide as recited in claim 14 wherein the hydrophilic polymer is a nonionic polymer (ie., starch, see the specification, page 8, second paragraph) as recited in claim 22 and hydrophilic polymer is a cellulose derivative as recited in claim 23, wherein the hydrophilic polymer is selected from the group consisting of polyacrylamide, polyethylene glycol, polyvinyl alcohol and saccharide as recited in claim 24, and wherein the aqueous solution contains the hydrophilic polymer in an amount of 0.1 to 2.0 vol. % (ie., 1% binding aid solution) as recited in claim 25.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have spotted an aqueous solution containing a hydrophilic polymer (ie., a binding aid) and a compound selected from the group consisting of the oligonucleotide and polynucleotide onto the solid carrier wherein said oligonucleotide or

polynucleotide has an amino group as recited in claim 14 in view of the prior art of Brown *et al.*, Cook, and Rudolph. One having ordinary skill in the art would have been motivated to do so because Rudolph has successfully loaded RNA or DNA probes with a binding aid onto a solid support and suggests that "the binding aids of this invention do not themselves attach or link the biological agent to the support, but serve to localize the biological agent so that it becomes immobilized in the desired position. This localization also ensures that the entire deposited quantity of biological agent is immobilized on the support" (see column 3, second paragraph) while Cook suggests that certain modifications (ie., an amino group) to the 3' or 5' terminus of oligonucleotides would improve the pharmacological properties of the oligonucleotides (see column 3, lines 31-35), and the simple replacement of one kind of oligonucleotide (i.e., the PCR product taught by Brown *et al.,*) from another kind of oligonucleotide (i.e., the oligonucleotide having an amino group on its 3' or 5' taught by Cook) during the process for performing the method recited in claim 14 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the PCR product taught by Brown *et al.,* and the oligonucleotide taught by Cook have the same intended use (ie., loading onto a solid support).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07, and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

9. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown *et al.,* in view of Cook as applied to claims 14 and 16-18 above, and further in view of Running *et al.,* (BioTechniques, 8, 276 and 279, 1990).

The teachings of Brown *et al.,* and Cook have been summarized previously, *supra.*

Brown *et al.,* and Cook do not disclose that the oligonucleotide or the polynucleotide is fixed to the solid carrier at its one end portion.

Running *et al.,* teach to activate a nucleic acid having an amino group (ie., N-LCA DNA) and couple the activated nucleic acid to a solid support coated with poly-l-lysine by its one end (see pages 276 and 279 and Figure 1).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 15 wherein the oligonucleotide or polynucleotide is fixed to the solid carrier at its one end portion in view of the prior art of Brown *et al.,* Cook, and Running *et al.*. One having ordinary skill in the art would have been motivated to do so because Running *et al.,* have successfully activate a nucleic acid having an amino group (ie., N-LCA DNA) and couple the activated nucleic acid to a solid support coated with poly-l-lysine by its one end and the simple replacement of one kind of oligonucleotide (i.e., the oligonucleotide having an amino group taught by Cook) from another kind of oligonucleotide (i.e., the oligonucleotide having an amino group taught by Running *et*

al.,) during the process for performing the method recited in claim 15 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the oligonucleotide taught by Cook and the oligonucleotide taught by Running *et al.,* have the same intended use (ie., loaded onto a solid support) and coupling an oligonucleotide having an amino group to a solid support coated with poly-l-lysine using the method taught by Running *et al.,* would enhance stability of the nucleic acid immobilized on the solid support because, after activation, the oligonucleotide taught by Running *et al.,* has an aldehyde group in its one end that forms a complex with poly-l-lysine on the solid support.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07, and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

10. Applicant's arguments with respect to claims 14-25 filed on September 19, 2005 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Frank Lu
Primary Examiner
January 12, 2006